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(1) (a) Tumor Inhibitors. 95. Part 94: S. M. Kupchan and R. M. Schubert, *Science*, in press. (b) This investigation was supported by grants from the National Cancer Institute (CA-11718 and CA-11760) and the American Cancer Society (Ci-102J), and a contract with the Division of Cancer Treatment, National Cancer Institute (N01-CM-12099). A. L. D. was a National Institutes of Health Postdoctoral Fellow, 1972–1974.

(2) Roots were collected in Oahu, Hawaii, in March 1972. The authors acknowledge with thanks receipt of the dried material from Dr. R. T. Hirano, Harold L. Lyon Arboretum, University of Hawaii, under a program supported by the National Cancer Institute.

(3) Cytotoxicity (Table I) and *in vivo* activity were assayed under the auspices of the National Cancer Institute. The procedures were those described in *Cancer Chemother. Rep.*, **25**, 1 (1962).

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Nucleosides. LXXXVII. Total Synthesis of Pentopyranine A, an α-L Cytosine Nucleoside Elaborated by *Streptomyces griseochromogenes*[1]

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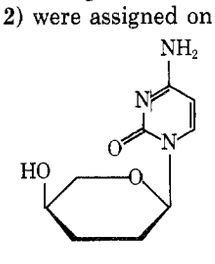
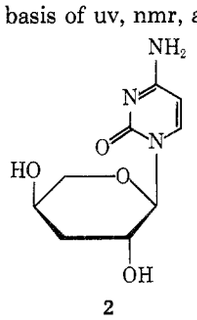
Received March 27, 1974

The nucleoside 1-(2,3-dideoxy-α-L-*glycero*-pentopyranosyl)cytosine (1) was synthesized by a series of reactions from tri-*O*-acetyl-L-arabinopyranosyl bromide. The identity of 1 with the naturally occurring pentopyranine A was established by ir, uv, and mass spectral comparisons. The synthetic sequence and physicochemical data for 1 reported herein provide confirming evidence for the structure previously assigned to pentopyranine A.

Two cytosine nucleosides, pentopyranine A and C, have been isolated by Seto, *et al.*,[2] from the fermentation broth of *Streptomyces griseochromogenes*, a blasticidin S producing microorganism.[3] The structures of these nucleosides (1 and 2) were assigned on the basis of uv, nmr, and mass



1
pentopyranine A

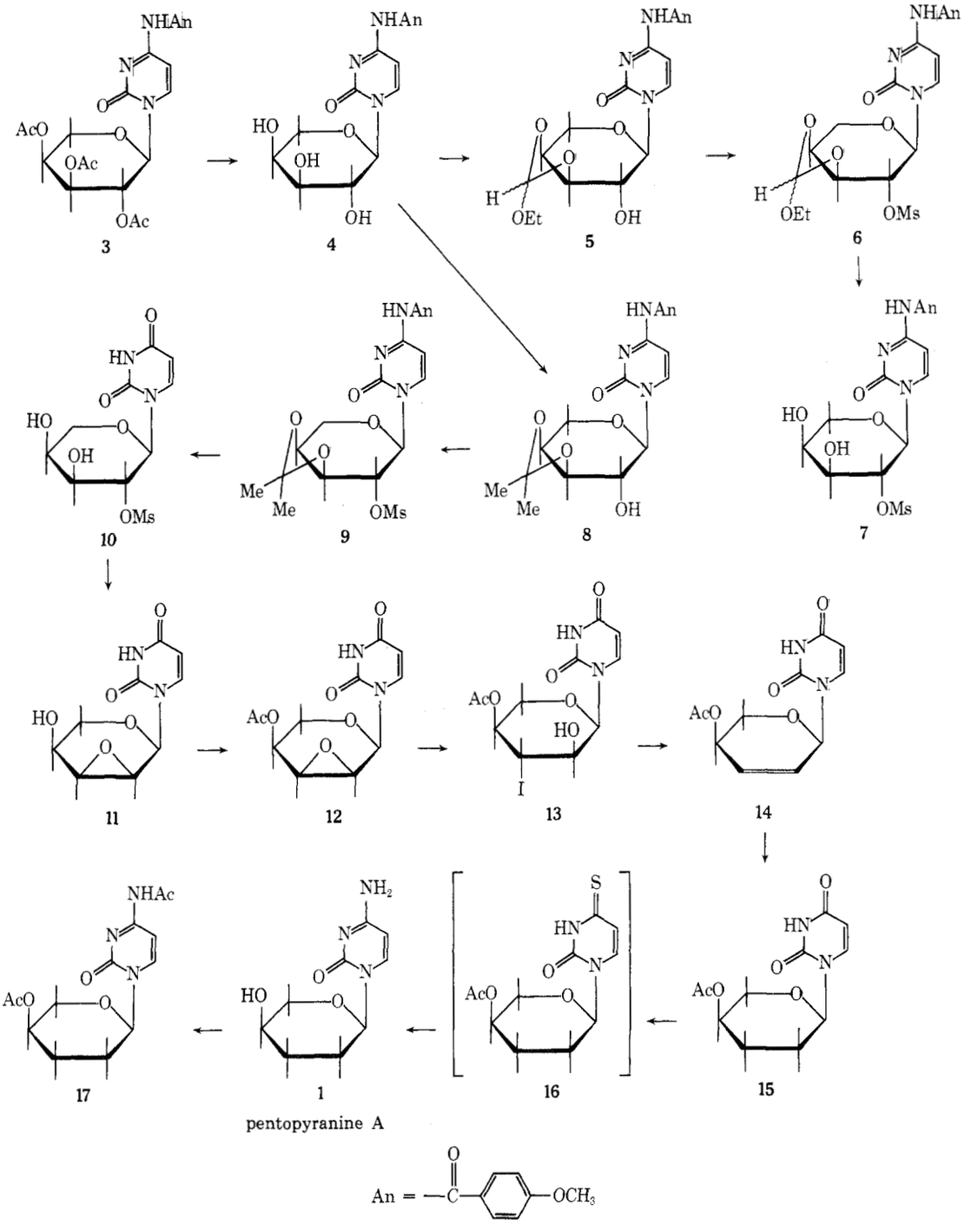


2
pentopyranine C

spectral evidence of these and their acetyl derivatives.[2] Pentopyranine A and C are the first naturally occurring nucleosides possessing the α-L configuration. Recently,[4] we reported the total synthesis of pentopyranine C, 1-(3-deoxy-α-L-*threo*-pentopy ranosyl)cytosine (**2**), from 3-deoxy-1,2:5,6-di-*O*-isopropylidene-α-D-*xylo*-hexofuranose. In this paper we describe the total synthesis of 1-(2,3-dideoxy-α-L-*glycero*- pentopyranosyl)cytosine (**1**) from L-arabinose and its identity with pentopyranine A.

Condensation of tri-*O*-acetyl-L-arabinosyl bromide with N^4-anisoylcytosine in nitromethane in the presence of mercuric cyanide[5] gave the protected nucleoside **3** in crystalline form. Treatment of **3** with sodium methoxide in methanol selectively removed the acetyl groups to afford nucleoside **4** in ~70% yield. Isopropylidenation of **4** gave pure **8** which precipitated from the reaction mixture in high yield. After mesylation of **8**, the product **9** was isolated and treated with aqueous acetic acid at room temperature to remove the isopropylidene group.[6] It was found, however, that under these conditions hydrolytic deamidation of **9** occurred to a considerable extent. Therefore, the reaction mixture was refluxed in 80% acetic acid to complete the deamidation reaction[7] from which uracil nucleoside derivative **10** was obtained in good yield.

Treatment of **10** with sodium methoxide in methanol gave the epoxide **11**. After acetylation of **11**, the product **12** was treated with sodium iodide in a mixture of acetic acid



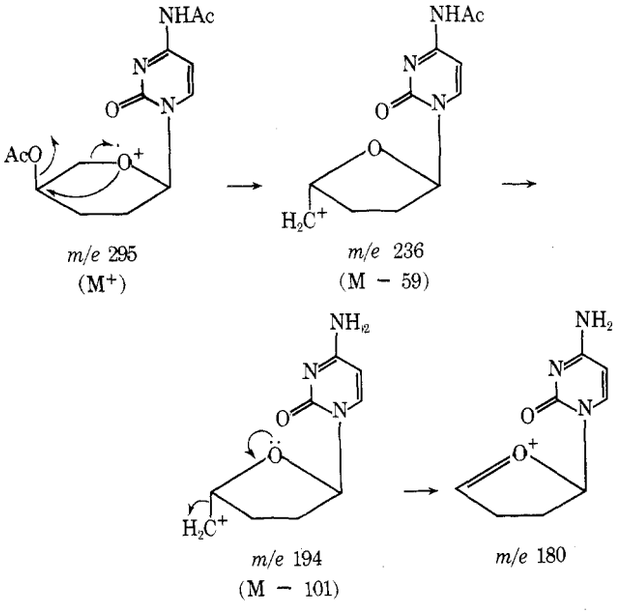
and acetone.[8,9] The crystalline iodohydrin **13** thus obtained was converted into the olefinic sugar derivative **14** by treatment with mesyl chloride in pyridine.[8,9] Hydrogenation of **14** gave the crystalline 2′,3′-dideoxy nucleoside derivative **15** in good yield. Thiation of **15** with phosphorus pentasulfide in dioxane[10] gave a syrupy product which resisted crystallization even after chromatographic purification. The chromatographically homogeneous thiouracil derivative **16** was treated with methanolic ammonia and the cytosine nucleoside **1** was obtained in good yield. Although the melting point of this compound (browning at ~235° and effervescence at 253–256°) is different from that reported[2] for pentopyranine A (mp 258° dec), a direct comparison of this compound with an authentic sample of pentopyranine A showed them to be identical. The melting point (mixture melting point showed no depression), uv, and ir characteristics were the same for both the synthetic and natural products. Acetylation of **1** afforded a cyrstalline diacetate (**17**) which was identical in all respects (melting point, uv, ir, and nmr spectra) with the diacetate prepared from pentopyranine A. These data not only provide proof of the identity of **1** with the natural product but also, by virtue of the route employed for its total synthesis, strongly support the assignment of the structure given by Seto, *et al.*,[2] for pentopyranine A.

It is noted that in the total synthesis shown, a cytosine nucleoside (**3–9**) was converted to uracil derivatives (**10–15**) and finally converted to a cytosine nucleoside (**1**) by thiation to **16**. This rather lengthy route was necessitated by the susceptibility of the 4-acylamino group of **9** to acid hydrolysis conditions required for deketalization. The introduction of the more readily removable group at the 3′,4′ positions was attempted. Thus treatment of **4** with ethyl orthoformate in DMF in the presence of hydrogen chloride[11]

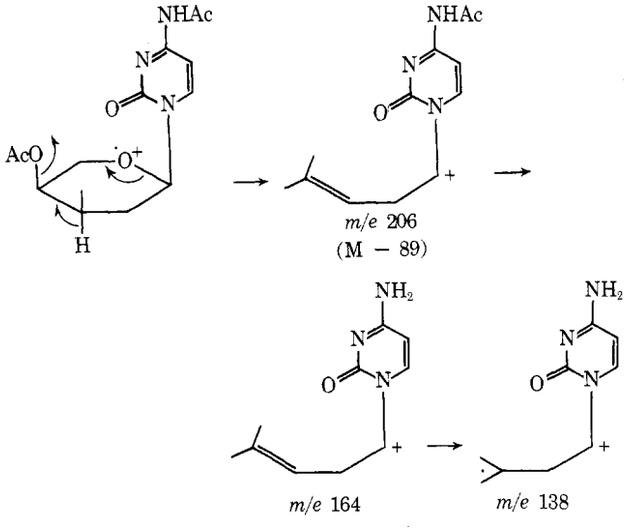
afforded a syrupy mixture of the 3′,4′-ethoxymethylidene diastereoisomers (**5**), from which one of them was obtained in crystalline form. Mesylation of crystalline **5** yielded the 2′-mesylate **6** in good yield. Removal of the ethoxymethylidene grouping was readily achieved by brief acid treatment to afford **7**. Attempts to convert **7** to the 2′,3′-epoxide by treatment with sodium methoxide gave a mixture of several products, none of which was formed in predominant amounts. This approach was therefore abandoned.

Data obtained from a mass spectral investigation of synthetic pentopyranine A and its diacetate **17** are fully consistent with the structure assigned. In the high-mass region, synthetic **1** shows peaks at *m/e* 211 (M^+), 112 (B + 2), 111 (B + 1), and 100 (S).[12] Ion peaks corresponding to (M − 30) and (B + 30) are absent, indicating that the compound contains neither a terminal hydroxymethyl function nor a hydroxyl group at C-2′.[13] More definitive information was obtained from the mass spectrum of the diacetate **17**, which exhibits fragmentation peaks which are best rationalized by the following sequences.

Sequence A



Sequence B



Sequence A requires a pyranoid → furanoid rearrangement. Such a rearrangement has been observed in the mass spectra of 2,3-diacetoxypyran[14] and of several hexopyranose pentaacetates.[15] The ion peaks at *m/e* 295 (M^+), 154 (BA + 2), 153 (BA + 1), and 143 (S) as well as those listed in sequences A and B are consistent only with the presence of an acetoxy function at C-4′ of a 2,3-dideoxypentopyranosyl sugar moiety.

Experimental Section

General Procedure. Melting points were determined on a Thomas-Hoover apparatus (capillary method) and are corrected. The nmr spectra were recorded on a Varian A-60 or XL-100 using TMS as internal standard. Chemical shifts are reported in parts per million (δ) and signals are described as s (singlet), d (doublet), t (triplet), and q (quartet). Values given for coupling constants are first order. Thin layer chromatography (tlc) was performed on silica gel GF_{254} (Merck), developed in a chloroform–methanol (9:1) system, and spots were detected by uv absorbance or by spraying with 20% v/v sulfuric acid–ethanol and heating. Microanalyses were performed by Galbraith Laboratories, Inc., Knoxville, Tenn.

N^4-Anisoyl-1-(tri-*O*-acetyl-α-L-arabinosyl)cytosine (3). A suspension of N^4-anisoylcytosine (37.5 g, 0.15 mol) and mercuric cyanide (75 g, 0.3 mol) in nitromethane (1700 ml) was dried by azeotropic distillation of approximately 200 ml of the solvent. To the stirred suspension was added a dichloromethane solution (~500 ml) of tri-*O*-acetyl-L-arabinopyranosyl bromide which was prepared by the following procedure.

Tetra-*O*-acetyl-β-L-arabinopyranose (95 g, 0.3 mol) was shaken in ~30% hydrogen bromide in acetic acid (800 ml) until a clear solution was obtained. The solution was left standing for 15 min, then partitioned between dichloromethane (1000 ml) and ice–water (1000 ml). The organic layer was separated and washed with cold water (2 × 1000 ml), saturated sodium bicarbonate solution (500 ml), and water (1000 ml), then dried over sodium sulfate. The solvent was concentrated to ~500 ml.

The condensation reaction mixture was refluxed for 2 hr, during which time the dichloromethane was removed by distillation. After cooling, the precipitate (N^4-anisoylcytosine, 19 g, 50%) was removed by filtration, and the filtrate was evaporated to near dryness. The residue was shaken with a mixture of dichloromethane (500 ml) and 30% potassium iodide solution (500 ml). The organic layer was separated and extracted with 30% potassium iodide solution (500 ml) and water (2 × 500 ml) and dried over sodium sulfate. The solution was concentrated to ~200 ml *in vacuo* and cooled to 0° overnight. Compound **3** (32 g, 43%) was obtained as colorless, fine needles: mp 227–228°; $[\alpha]^{27}D$ +53° (*c* 0.9, dioxane); nmr (DMSO-d_6), OAc, δ 1.93 (s, 3 H), 1.98 (s, 3 H), 2.18 (s, 3 H); OCH_3, δ 3.86 (s, 3 H); H-1′, δ 6.10 (d, 1 H, $J_{1',2'}$ = 8.0 Hz); uv λ_{max} (MeOH) 289 nm, λ_{min} (MeOH) 242 nm.

Anal. Calcd for $C_{23}H_{25}N_3O_{10}$: C, 54.87; H, 5.01; N, 8.35. Found: C, 54.93; H, 5.31; N, 8.12.

N^4-Anisoyl-1-(α-L-arabinopyranosyl)cytosine (4). Compound **3** (15 g, 0.03 mol) was dissolved in dioxane (150 ml) and the solution was diluted with methanol (150 ml). To the solution was added dropwise 1 *M* sodium methoxide in methanol (5 ml). After 15 min the mixture was neutralized with Dowex 50 (H^+, 20 ml). The resin was removed by filtration and the filtrate was concentrated to ~50 ml. Water (150 ml) was added to the mixture, which was then concentrated to ~100 ml and cooled at 0°. Compound **4** (7.2 g, 65%) was obtained as colorless needles: mp 231–233°; $[\alpha]^{27}D$ +59° (*c* 1.3, DMF). The product analyzed best for a hydrate.

Anal. Calcd for $C_{17}H_{19}N_3O_7 \cdot H_2O$: C, 51.64; H, 5.35; N, 10.62. Found: C, 52.19; H, 5.31; N, 10.20.

This product was not further purified but used directly in the syntheses of **5** and **8**, both of which afforded correct analyses (see below).

N^4-Anisoyl-1-(3,4-*O*-ethoxymethylidene-α-L-arabinopyranosyl)cytosine (5). Compound **4** (2.0 g, 5.3 mmol) was dissolved in DMF (20 ml). To the solution was added triethyl orthoformate (2 ml) followed by 10 *M* hydrogen chloride in DMF (1 ml). After 2 hr, another charge of triethyl orthoformate (3 ml) and 10 *M* hydrogen chloride in DMF was added and the mixture was left overnight at room temperature. Solid sodium bicarbonate (4 g) was added and the mixture was stirred for 4 hr; then the insoluble inorganic material was removed by filtration. The filtrate was evaporated to a syrup from which crystals slowly separated. After 20 hr at room temperature, the mixture of syrup and crystals was triturated with ethanol (15 ml). The crystals were filtered and washed with ethanol (0.9 g, 39%): mp 211–212°; $[\alpha]^{27}D$ +69° (*c* 1.3, dioxane); nmr (DMSO-d_6) δ 1.15 (t, 3 H, CH_2CH_3), 3.58 (q, 2 H, CH_2CH_3), 3.85

(s, 3 H, OCH_3), 5.53 (d, 1 H, H-1′, $J_{1',2'}$ = 9.5 Hz), 6.02 (s, 1 H, ethoxymethylidene).

Anal. Calcd for $C_{20}H_{23}N_3O_8$: C, 55.42; H, 5.34; N, 9.70. Found: C, 55.42; H, 5.33; N, 9.63.

N^4-Anisoyl-1-(3,4-*O*-ethoxymethylidene-2-*O*-mesyl-α-L-arabinopyranosyl)cytosine (6). To a solution of compound **5** (433 mg, 1 mmol) in pyridine (5 ml) was added msyl chloride (0.6 ml) at 0°, and the mixture was kept at 0° for 16 hr, then partitioned between ice-cold water (30 ml) and dichloromethane (30 ml). The organic layer was separated, washed with 30 ml each of water, sodium bicarbonate, and water, and then dried over sodium sulfate. The solution was evaporated to dryness and the residue was dissolved in dichloromethane (~1 ml); then the solution was diluted with ethanol (~4 ml). Compound **6** crystallized as pale yellow needles (452 mg, 88%): mp 173° (sintered), 174–177° (effervesced); $[\alpha]^{27}D$ +100° (*c* 1.3, $CHCl_3$); nmr (DMSO-d_6) δ 1.23 (t, 3 H, CH_2CH_3), 3.21 (s, 3 H, OMs), 3.63 (q, 2 H, CH_2CH_3), 3.87 (s, 3 H, OCH_3), 5.97 (s, 1 H, ethoxy*methylidene*), 5.97 (d, 1 H, H-1′, $J_{1',2'}$ = 7.5 Hz).

Anal. Calcd for $C_{21}H_{25}N_3O_{10}S$: C, 49.31; H, 4.93; N, 8.22; S, 6.27. Found: C, 49.45; H, 4.92; N, 7.99; S, 5.88.

N^4-Anisoyl-(2-*O*-mesyl-α-L-arabinopyranosyl)cytosine (7). To a solution of **6** (382 mg, 0.75 mmol) in dioxane (15 ml) was added 1 *N* HCl (4 ml) with stirring. After 25 min, the mixture was diluted with ethanol (46 ml) and the solvent was removed *in vacuo* below 40°. The residue was coevaporated several times with ethanol until pale yellow microcrystals were obtained. After one recrystallization from ethanol, **7** was obtained as colorless, fine needles: mp 205° (sintered), 208–209° (effervesced); $[\alpha]^{27}D$ +47° (*c* 1.3, pyridine); nmr (DMSO-d_6) δ 3.20 (s, 3 H, mesyl CH_3), 4.79 (t, 1 H, H-2′, $J_{1',2'} \simeq J_{2',3'} \simeq$ 9.0 Hz), 5.91 (d, 1 H, H-1′, $J_{1',2'} \simeq$ 9.0 Hz).

Anal. Calcd for $C_{18}H_{21}N_3O_9S$: C, 51.07; H, 5.00; N, 9.93. Found: C, 50.77; H, 5.21; N, 10.12.

N^4-Anisoyl-(3,4-*O*-isopropylidene-α-L-arabinopyranosyl)cytosine (8). A mixture of **4** (12 g, 0.032 mol), *p*-toluenesulfonic acid (2 g), and 2,2-dimethoxypropane (20 ml) in acetone (480 ml) was vigorously stirred for 24 hr. Compound **8** (7.5 g) separated as colorless needles which were filtered and washed with acetone: mp 230–231°; $[\alpha]^{27}D$ +78° (*c* 1.3, DMF); nmr (DMSO-d_6) δ 1.24 (s, 3 H, isopropylidene CH_3), 1.54 (s, 3 H, isopropylidene CH_3), 3.87 (s, 3 H, OCH_3), 5.54 (d, 1 H, H-1′, $J_{1',2'}$ = 9.5 Hz).

Anal. Calcd for $C_{20}H_{23}N_3O_7 \cdot H_2O$: C, 55.17; H, 5.79; N, 9.65. Found: C, 55.21; H, 5.95; N, 9.67. The presence of 1 mol of water of crystallization was shown by the nmr spectrum.

To the combined filtrate and washings was added solid sodium bicarbonate (3 g) and the mixture was stirred for 5 hr. Insoluble solid was filtered and washed with a small amount of acetone. the solid was suspended in water (40 ml), stirred for 1 hr, and then filtered and dried to give additional product **8** (3.8 g, mp 229–231°).

N^4-Anisoyl-(3,4-*O*-isopropylidene-2-*O*-mesyl-α-L-arabinopyranosyl)cytosine (9). A mixture of **8** (7.5 g, 0.018 mol) in pyridine (100 ml) was cooled in an ice bath. Mesyl chloride (3 ml) was added to the mixture with stirring. After 4 hr, the reaction mixture was poured into a mixture of ice and water (500 ml), and then the mixture was extracted with chloroform (2 × 250 ml). The combined chloroform extracts were washed with water (250 ml), sodium bicarbonate solution (2 × 250 ml), and water (250 ml), and then dried over sodium sulfate. The solution was concentrated to dryness and the residue was coevaporated several times with ethanol until a crystalline residue was obtained. The residue was recrystallized from ethanol to give colorless needles: 7.2 g (81%); mp 199–200° dec; $[\alpha]^{27}D$ +102° (*c* 1.1, DMF); nmr (DMSO-d_6) δ 1.37 (s, 3 H, isopropylidene CH_3), 1.58 (s, 3 H, isopropylidene CH_3), 3.21 (s, 3 H, SCH_3), 3.85 (s, 3 H, OCH_3), 5.93 (d, 1 H, H-1′, $J_{1',2'}$ = 8.5 Hz).

Anal. Calcd for $C_{21}H_{25}N_3O_9S$: C, 50.90; H, 5.09; N, 8.48; S, 6.47. Found: C, 50.86; H, 4.78; N, 8.50; S, 6.51.

1-(2-*O*-Mesyl-α-L-arabinopyranosyl)uracil (10). Compound **9** (7.0 g, 0.014 mol) was dissolved in warm acetic acid (320 ml) and the solution was cooled to room temperature. Water (80 ml) was added to the solution and the mixture was stirred overnight and then refluxed for 3 hr. Evaporation of the solvent and subsequent addition and evaporation of toluene (3 × 100 ml) gave a semisolid residue which was triturated with chloroform (2 × 30 ml). The residue was crystallized from ethanol to give **10** as colorless, hard needles: 2.2 g (73%); mp 202–205° dec (effervesced); $[\alpha]^{27}D$ +79° (*c* 1.3, DMF).

1-(2,3-Anhydro-α-L-ribopyranosyl)uracil (11). A mixture of **10** (1.8 g, 5.6 mmol), 1 *M* sodium methoxide in methanol (7 ml), and ethanol (20 ml) was refluxed for 45 min and then cooled to room temperature. The precipitates were removed by filtration and the filtrate was evaporated to dryness. The residue was dissolved in a 4:1 chloroform–methanol mixture (~5 ml) and chromatographed over a silica gel G column (50 g, 7 × 4 cm diameter) using 4:1 chloroform–methanol system as the eluent. The uv-absorbing fractions were collected and concentrated to dryness. The crystalline residue was recrystallized from ethanol: 970 mg (77%); mp 164–165°; $[\alpha]^{27}D$ +15° (*c* 0.8, pyridine).

Anal. Calcd for $C_9H_{10}N_2O_5$: C, 47.79; H, 4.46; N, 12.39. Found: C, 47.81; H, 4.51; N, 12.23.

1-(4-*O*-Acetyl-2,3-anhydro-α-L-ribopyranosyl)uracil (12). Acetic anhydride (1 ml) was added to a solution of **11** (800 mg, 3.5 mmol) in pyridine (16 ml). The mixture was stirred overnight, after which it was treated with ethanol (10 ml). After evaporation of the mixture, the residue was triturated with ether (20 ml) and then crystallized from ethanol to give colorless needles: 721 mg (75%); mp 238–244° dec; $[\alpha]^{27}D$ −27° (*c* 1.4, pyridine).

Anal. Calcd for $C_{11}H_{12}N_2O_6$: C, 49.26; H, 4.51; N, 10.44. Found: C, 49.39; H, 4.47; N, 10.20.

1-(4-*O*-Acetyl-3-deoxy-3-iodo-α-L-xylopyranosyl)uracil (13). A mixture of **12** (540 mg, 2 mmol), sodium iodide (1.7 g), sodium acetate (90 mg), and acetic acid (2.8 ml) in acetone (10 ml) was refluxed gently for 30 min. Evaporation of the solvent and subsequent addition and evaporation of toluene (2 × 10 ml) gave a solid residue which was then shaken with a mixture of water (20 ml) and chloroform. Slightly yellowish needles crystallized out. They were filtered and washed with a small amount of chloroform (624.5 mg, 80%): mp 193–195°, 198–199° (effervesced); $[\alpha]^{27}D$ +24° (*c* 1.2, pyridine).

Anal. Calcd for $C_{11}H_{13}N_2O_6I$: C, 33.33; H, 3.28; N, 7.07; I, 32.07. Found: C, 32.94; H, 3.67; N, 6.95; I, 32.03.

1-(4-*O*-Acetyl-2,3-dideoxy-α-L-*glycero*-pent-2-enopyranosyl)uracil (14). To a solution of **13** (590 mg, 1.5 mmol) in pyridine (5.5 ml) was added mesyl chloride (0.4 ml, 5.2 mmol) and the mixture was kept at room temperature for 16 hr. The very dark colored reaction mixture was partitioned between chloroform (20 ml) and water (20 ml). The aqueous layer was washed with chloroform (20 ml). The combined chloroform solutions were washed successively with 20 ml each of water, 0.1 *M* sodium thiosulfate (4 ×), and water, dried over sodium sulfate, and evaporated. The residue was coevaporated several times with ethanol until crystallization occurred. The product was recrystallized from ethanol to give fine needles: 173 mg (52%); mp 153–154°; $[\alpha]^{27}D$ −84° (*c* 1.1, dioxane).

Anal. Calcd for $C_{11}H_{12}N_2O_5$: C, 52.38; H, 4.80; N, 11.11. Found: C, 52.14; H, 4.68; N, 10.98.

An additional amount (72 mg, mp 151–153°) was obtained from the mother liquor.

1-(4-*O*-Acetyl-2,3-dideoxy-α-L-*glycero*-pentopyranosyl)uracil (15). Compound **14** (222 mg, 1 mmol) was dissolved in dioxane (10 ml) and hydrogenated over 10% palladium on carbon (~25 mg) at room temperature and atmospheric pressure. After 1 mol of hydrogen was taken up, the catalyst was removed by filtration and the filtrate was concentrated to dryness. The residue was crystallized from ethanol to give colorless needles: 156 mg (71%); mp 146–147°; $[\alpha]^{27}D$ +39° (*c* 0.9, dioxane).

Anal. Calcd for $C_{11}H_{14}N_2O_5$: C, 51.97; H, 5.55; N, 11.02. Found: C, 51.89; H, 5.57; N, 11.18.

1-(4-*O*-Acetyl-2,3-dideoxy-α-L-*glycero*-pentopyranosyl)-4-thiouracil (16). To a stirred solution of **15** (115 mg, 0.5 mmol) in dioxane (8 ml) was added phosphorus pentasulfide (112 mg, 0.5 mmol) and the mixture was refluxed for 45 min. A second charge of phosphorus pentasulfide (82 mg) was then added and heating was resumed for another 45 min. Only one spot (less polar than **15**) was detected on tlc by this time. The mixture was cooled and the supernatant was decanted from a small amount of insoluble material and evaporated to dryness. The residue was triturated with a small amount (~5 ml) of warm water (~60°) for a few minutes, and the mixture was extracted with chloroform (2 × 5 ml). The combined chloroform extracts were washed with sodium bicarbonate and water (5 ml each) and dried over sodium sulfate. After removal of the solvent by evaporation, the residue (98 mg, 82%) was dissolved in ~2 ml of chloroform and spotted on a glass plate (20 × 20 cm) coated with silica gel PF_{254} and developed in a chloroform–methanol (9:1) system. The uv-absorbing band was removed and extracted with chloroform–methanol (9:1). After evaporation of the solvent, 72 mg of yellow syrup was obtained. The syrup was used directly in the next step.

1-(2,3-Dideoxy-α-L-*glycero*-pentopyranosyl)cytosine (1). Compound **16** (52 mg, 0.2 mmol) was dissolved in ~2 ml of methanolic ammonia (saturated at 0°) in a test tube which was sealed

and heated at 100° for 48 hr in a steel container. The dark yellow reaction mixture was concentrated to dryness and the residue was mixed with water (2 ml) and decolorized with charcoal Darco 60. The colorless aqueous solution was evaporated to dryness and coevaporated several times with ethanol. The residue was triturated twice with chloroform (2 ml each) and the residue was finally crystallized from water–ethanol to give colorless needles: 27.4 mg (60%); mp ~235° (browning), 253–256° (effervesced).

N^4-Acetyl-1-(4-*O*-acetyl-2,3-dideoxy-α-L-*glycero*-pentopyranosyl)cytosine (17). A mixture of 1 (17 mg), acetic anhydride (0.5 ml), and pyridine (2 ml) was kept at room temperature for 16 hr. The reaction was stopped by addition of water (5 ml) followed by extraction with chloroform (2 × 5 ml). The organic extracts were washed with 5 ml each of water, saturated sodium bicarbonate solution, and water and dried over sodium sulfate. After removal of the solvent, traces of pyridine were removed by coevaporation of ethanol. The crystalline residue was recrystallized from ethanol, 7 mg, mp 200–202°, unchanged on admixture with an authentic sample.[2]

Acknowledgment. The authors express their appreciation to Dr. H. Seto of the Institute of Applied Microbiology of the University of Tokyo for a sample of pentopyranine A. We also thank Dr. Y. Shimizu of the University of Rhode Island, School of Pharmacy, for the recording of mass spectra. We are indebted to Mr. R. Grulich of Ciba-Geigy Co., Ardsley, N. Y., for determination of some of the nmr spectra on a Varian XL-100 spectrometer, and to Mr. M. J. Olsen of this Institute for nmr spectra on a Varian A-60.

Registry No.—**1**, 39057-02-8; **3**, 51838-76-7; **4**, 51820-58-7; **5**, 51820-59-8; **6**, 51820-60-1; **7**, 51820-61-2; **8**, 51820-62-3; **9**, 51820-63-4; **10**, 51820-64-5; **11**, 51838-77-8; **12**, 51820-65-6; **13**, 51838-78-9; **14**, 51820-66-7; **15**, 51820-67-8; **16**, 51820-68-9; **17**, 51820-69-0; N^4-anisoylcytosine, 51820-70-3; tri-*O*-acetyl-L-arabinopyranosyl bromide, 51830-02-5.

References and Notes

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Electrolytic Decarboxylation Reactions. I. Electrosyntheses of γ-Substituted Butyrolactones and γ-Substituted α,β-Butenolides from γ-Substituted Paraconic Acids

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Received March 26, 1974

The product-selective electrolytic decarboxylation of γ-substituted paraconic acids has been studied (1) in dry methanol using sodium methoxide by addition of iron powder or ferric nitrate on platinum electrodes, (2) in dry methanol using sodium methoxide on carbon rod electrodes, and (3) in a mixed solvent of triethylamine–pyridine–water on carbon rod electrodes. Conditions 1 and 2 resulted in exclusive formation of γ-substituted butyrolactones in 80–99% yields, whereas condition 3 provided α,β-unsaturated butenolides in 70–90% yields. By means of the butenolide synthesis *dl*-3-carboxy-8-hydroxy-Δ^3-menthene γ-lactone, a key intermediate for the preparation of *dl*-menthone, could be prepared.

The value of non-Kolbe type electrolytic reactions for the preparation of synthetic intermediates has been discussed recently.[1] Choices of electrodes, solvents, supporting electrolytes, additives, etc., in relation to product selectivity have been the subject of several investigations.[2] We report herein the product-selective electrolytic decarboxylation reaction of γ-substituted paraconic acids (1), which led to the discovery of a chemically controlled electrolysis.

Preliminary electrolysis[3] of **1** [R_1, R_2 = $-(CH_2)_5-$][4] in dry methanol using sodium methoxide as a supporting electrolyte on platinum electrodes (Table I, run 1) afforded lactone derivatives of **2** (32%), **3** (49%), and **4** (10%). However, addition of iron powder or ferric nitrate in the electrolytic